01 - CERVICAL CANCER

GYAN VAHINI

FROM

FOGSI, FOOD DRUGS & MEDICOSURGICAL EQUIPMENT COMMITTEE

January- 2025

Message From Dr. Sunita Tandulwadkar

Dr. Sunita Tandulwadkar

President FOGSI-2025

Dear Colleagues, As we embark on a new year filled with renewed purpose and dedication, I am delighted to connect with you through the inaugural edition of GYAN VAHINI—our Food, Drugs, and Medicosurgical Equipment Committee's initiative, aptly named as a 'vehicle of knowledge'. This month's focus on cervical cancer holds special significance, as it aligns with one of my key presidential projects,**'Do Teeke Zindagi Ke', aimed at driving awareness and action towards preventing cervical cancer through vaccination and timely screening. I deeply appreciate Dr. Asha Jain's initiative in bringing this crucial topic to the forefront, reinforcing our commitment to ensuring a cancer-free future for women across India. Cervical cancer is not just a disease; it is a challenge that we, as medical professionals, have the power to eliminate through education, advocacy, and action. With the right knowledge, vaccination programs, technological advancements, and robust screening initiatives, we can significantly reduce the burden of this preventable disease. Let's stand together in this mission—to educate, to motivate, and to advocate for every woman's right to a healthier, cancer-free life. I look forward to the continued impact of GYAN VAHINI in empowering our community with vital knowledge and fostering meaningful change.

With best wishes,
Dr. Sunita Tandulwadkar
President, FOGSI

Message from Dr Abha Singh

Dr. Abha Singh
Vice President FOGSI-2025

Dear Fogsians ,
Wishing you all a very Happy New Year .
This Gyan Vahini Focus is being published by Food , drugs & Medico surgical equipment committee focuses on “Prevention and early detection of cervical cancer”.
Cervical Cancer is one of the most common cancer in women globally with 660,000 new cases and 3,50000 deaths reported in 2022.It is a public health problem and a cause of concern due to associated high maternal deaths . So, joint efforts are required with a multipronged approach.
The causative agent is HPV infection during sexual debut . The persistence of HPV infection leads to cellular changes suggestive of underlying disease and if not treated may cause cervical cancer.
However, creating awareness and screening with Pap smear can detect the early cellular changes and HPV testing should be done. If detection is done in early stages treatment is possible.
Another strategy to eliminate this disease is vaccination of adolescents , increasing the immunogenicity by“Do Tike Zindagi Ke ’’, A FOGSI Project.
Moreover, WHO has come up with a strategy to eliminate cervical cancer by 2030 by slogan 90,70,90. Vaccinate 90 % adolescents, Screen 70% women and treat 90 % women detected to have early disease.
So this Gyan Vahini published under Dr Asha Jain will enable to spread awareness about this preventable disease among all health care professionals.
I congratulate all the contributors of this bulletin in their effort to spread awareness and taking a step to eliminate this deadly disease.

Happy reading!

Message from Dr Suvarna Khadilkar

Dr. Suvarna Khadilkar
Secretary General FOGSI-2025

Dear Esteemed Members,

Greetings to each and every one of you. It is both a privilege and an honour to have been installed as the 17th Secretary General of FOGSI on January 9, 2025 during the Diamond Jubilee(75th) year of FOGSI. As we enter in the new year 2025, I extend my heartfelt wishes for health and prosperity to you and your loved ones.

Let me take this opportunity to introduce you to the first edition of GYAN VAHINI, an initiative of our Food, Drugs, and Medicosurgical Equipment Committee, which is chaired by Dr. Asha Jain. This issue focuses on cervical cancer and covers important topics such as Guarding Against Cervical Cancer, Innovating Surgery, The Digital Edge, and Cervical Cancer Vaccination.

Every year, about 1,20,000 women in India get uterine cervical cancer. This represents 15.2% of the global fatality rate from cervical cancer. The most frequent HPV-related cancers in India were cervical cancer (87.6%) and oropharyngeal cancer (63.2%) in females and males, respectively.

Eighty percent of HPV-related cancers are cervical cancers, which can be prevented with the HPV vaccine. The risk of HPV infection and its persistence increases with age.

FOGSI encourages gynaecologists in India to actively participate in our "DO TIKE JINDEGI KE" campaign, which aims to vaccinate girls aged 9 to 14 against HPV and help reduce cervical cancer rates. Additionally, we want to work together to support women aged 15 to 45 who may have missed their vaccine, ensuring they receive the three doses needed for their protection.

Together, we will raise awareness, inspire hope, and provide unwavering support to Cancer awareness. Let us collaborate to combat cancer and advocate for a healthier future, we can make a significant impact in this important endeavour.

I will work towards betterment of healthcare of women and organisation and my aim is to Support, Strengthen, Sustain and Stabilise FOGSI.

With best and warm wishes,
Dr. Suvarna Khadilkar
Secretary General, FOGSI

Dr. Asha Jain
Chairperson
FOGSI FDMSE Committee

FOREWORD

As Chairperson of the Food, Drugs, and Medicosurgical Equipment Committee, it is my pleasure to introduce the first edition of "Gyan Vahini," our monthly newsletter.

This issue focuses on the critical battle against cervical cancer, featuring pioneering research and innovative treatment strategies from our esteemed contributors.

I extend a special thank you to Dr. Sunita Tandulwadkar for her leadership and unwavering support, and encouragement to think different and the drive to get it done. She is a great asset to me in my first year as FOGSI Chairperson.

My heartfelt gratitude to Dr. Abha Singh, Dr. Suvarna Khadilkar and Dr. Ashwini Kale for their pivotal contributions to our initiatives.

Additionally, I express my deepest gratitude to the authors who have enriched this edition with their insights and expertise: Dr. Jyothi G.S., Dr. Vishnupriya KMN, Dr. Sugandha Goel, Dr. Rimpi Singla, Dr. Sandhya Rani Panigrahy, Dr. Renu Jain, Dr. Himleena Gautam, Dr. Okram Sarda Devi, and Dr. Ishan P. Shah. Your contributions are fundamental to our mission of disseminating knowledge and fostering innovation in healthcare.

A special acknowledgment is due to Dr. Ruche Bhargava, who not only contributed an article but also played a crucial role in compiling this insightful collection.

I also want to acknowledge our talented designer, Bhupendra, whose dedication and skill bring visual clarity and impact to the content we share.

Together, we are driving forward the agenda of medical excellence and patient care. Thank you to all our contributors and readers for your engagement and commitment to advancing healthcare outcomes.

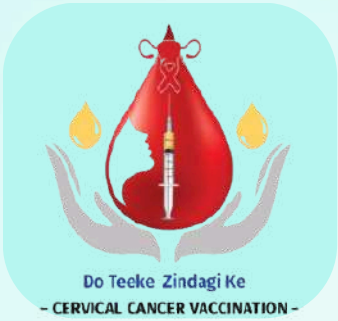
Dr Asha Jain
FOGSI CP- FDMSE Committee
2025-2027

"Know Your Numbers" is an ambitious health initiative.

- This project seeks to gather vital health data- Weight, Blood pressure, Blood Sugar Level with HbA1C, and Hemoglobin level -from women across India.
- By focusing on these key health indicators, the project aims to foster a proactive health management culture among women.
- The data collected will be instrumental in identifying prevalent health issues early and promoting interventions that can significantly reduce the incidence of che diseases.
- This initiative not only emphasizes the importance of regular health monitoring but also strives to empower women with the knowledge and tools needed to take charge of their health, ensuring they lead longer, healthier lives.
- Collect key health data: weight, blood pressure, blood sugar, HbA1C, and hemoglobin from women across India.
- Encourage proactive health management for early identification of prevalent health issues.
- Promote timely interventions to reduce chronic disease incidence.
- Empower women with knowledge and tools for better health and longevity.
- Gather vital health data: weight, blood pressure, blood sugar (HbA1C), and haemoglobin levels from women across India.
- Foster proactive health management among women.
- Identify prevalent health issues early and promote timely interventions.
- Reduce the incidence of chronic diseases through regular monitoring.
- Empower women with knowledge and tools for healthier, longer lives.

SURVEY FOR KNOW YOUR NUMBER (KYN) PROJECT

Do Teeke Zindagi Ke



As part of my upcoming tenure as the President of FOGSI, I am pleased to submit a proposal for a comprehensive training program on HPV vaccination, targeting 50,000 members of the Indian Medical Association (IMA). This initiative aligns with our shared goal of enhancing public health through preventive care, and I am confident that, with your support, we can make a significant impact in addressing cervical cancer awareness and prevention across India. 9-14 age group we will conduct the drive for increasing awareness of cervical cancer vaccination

Study on Understanding the Acceptance and Usage Patterns of Various Contraceptive Methods Among Women in India

Aims & Objectives

- To determine the prevalence of usage and type of contraceptives in various age groups across different demographic regions in India

- To identify whether contraception is used or not
- To identify the most commonly used contraception in men and women across India

Contraception

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01

Guarding Against Cervical Cancer: Vaccines and the Journey Towards Elimination

Author-Dr. Jyothi G S
MBBS, MD OBG, PGDMLE, FICOG, FICMCH
Professor and Head, Department of Obstetrics & Gynecology,
Ramaiah Medical College & Hospitals, Bengaluru 560 054.

Dr Saumya Singh
Junior Resident
Department of Obstetrics and Gynaecology,
Ramaiah Medical College and Hospitals,
Bengaluru 560 054

The HPV vaccine stands as a public health milestone, transforming the prevention of cervical cancer and other HPV-related diseases worldwide. Its journey began with groundbreaking research in the 1970s and 1980s, when Harald zur Hausen identified high-risk HPV types (16 and 18) as major causes of cervical cancer, earning him the Nobel Prize. Building on this discovery, Ian Frazer and Jian Zhou developed virus-like particles (VLPs) in the 1990s, forming the foundation of the first HPV vaccines. Approved in 2006, Gardasil 4 and Cervarix quickly demonstrated high efficacy in preventing HPV infections and precancerous lesions.

Australia played a leading role in making the HPV vaccine famous by launching one of the world's first national vaccination programs in 2007. Through a government-funded, school-based approach, initially targeting adolescent girls and later including boys, Australia achieved high vaccine uptake and a dramatic reduction in HPV infections and cervical precancerous lesions. By 2018, experts predicted that Australia could eliminate cervical cancer as a public health issue by 2035, setting a global example. The HPV vaccine's success, bolstered by robust public health campaigns and international collaboration, highlights its potential to eradicate HPV-related diseases, marking it as a triumph in preventive medicine.

HPV vaccines serve as a cornerstone in cervical cancer prevention by targeting the causative agents of the disease. Among the available vaccines, Gardasil 9, Gardasil 4, Cervarix, and Cervavac stand out:

- **Gardasil 9:** Offers protection against nine HPV types, including those causing 90% of cervical cancers. It is recommended for individuals aged 9-45 years.

- **Gardasil 4:** Covers HPV types 16 and 18 (responsible for 70% of cervical cancers) and types 6 and 11 (responsible for genital warts).

- **Cervarix:** Focuses on HPV types 16 and 18, particularly effective in resource-limited settings.

- **Cervavac:** India's first indigenous HPV vaccine, priced affordably to expand access in low-resource settings and covers HPV types 6,11,16 and 18

THE VISION FOR ELIMINATION :-

In 2020, the World Health Organization (WHO) introduced a Global Strategy to Accelerate the Elimination of Cervical Cancer, setting ambitious targets:

- 90% of girls fully vaccinated by age 15.
- 70% of women screened by age 35 and again by 45.
- 90% access to treatment for pre-cancerous lesions and invasive cancers.

Achieving these milestones could reduce cervical cancer cases by over 40% within a generation. For India, the affordability of Cervavac and ongoing outreach programs align with this global vision.

Global Availability and Accessibility

The implementation of the HPV vaccine varies significantly between high-income countries and low- and middle-income countries (LMICs). In high-income countries, the vaccine is integrated into routine immunization schedules and is often provided free or at low cost through national healthcare systems. In contrast, LMICs, which bear the highest burden of cervical cancer, face significant challenges, including the high cost of vaccines in private markets, supply shortages, and inadequate healthcare infrastructure, particularly in rural areas. Organizations like Gavi, the Vaccine Alliance, are working to address these disparities by funding vaccines and supporting delivery systems in LMICs, but achieving equitable access remains a critical global health priority.

Innovative Outreach Programs for HPV Vaccination Coverage in India

Given India's vast and diverse population, innovative outreach strategies are critical to scaling up HPV vaccination coverage.

1. School-Based Vaccination Programs

States like Punjab and Sikkim have successfully piloted school-based HPV vaccination drives, achieving coverage rates of over 80%.

Vaccinations are administered during routine health check-ups, ensuring minimal disruption to studies.

2. Anganwadi and ASHA Worker Involvement

Leveraging India's extensive network of Anganwadi workers and ASHA (Accredited Social Health Activists), who have established trust in communities, to promote HPV vaccines.

3. Free Vaccination Camps

Rural health centers, community halls, and places of worship to ensure accessibility.

Urban slums and informal settlements where healthcare access is limited. Cervavac rollout in several states includes mobile vaccination units traveling to underserved areas.

4. Public Awareness Campaigns

Campaigns by organizations like Cancer Patients Aid Association (CPAA) and Indian Cancer Society (ICS) focus on HPV awareness and prevention.

5. Partnership with NGOs and Corporates

NGOs like PATH India and Smile Foundation partner with local governments to implement vaccination drives and educational programs.

Corporates under Corporate Social Responsibility (CSR) initiatives fund free or subsidized vaccines and outreach campaigns.

6. Integration with Existing Health Programs

Like Mission Indradhanush, India's flagship immunization program, this reduces the need for standalone campaigns and increases the likelihood of vaccination uptake during routine health visits.

7. Digital Innovations for Outreach

The eVIN (Electronic Vaccine Intelligence Network) used for other vaccines could be adapted to manage HPV vaccine logistics.

HPV Vaccine	Protection	Dosage	Significance	Rollout
Gardasil 4 (Merck)	Targets HPV types 6, 11, 16, and 18	Two or three doses, based on age	Imported vaccine	Available in the private market
Gardasil 9 (Merck)	Covers nine HPV types for broader cervical cancer protection	Two or three doses, based on age	Imported vaccine with extended protection	Available in the private market
Cervarix (GSK)	Focuses on HPV types 16 and 18	Two or three doses based on age	Imported vaccine	Not available in the private market at present
Cervavac (Serum Institute of India	Targets HPV types 6, 11, 16, and 18	Two or three doses, based on age	First indigenous HPV vaccine launched in 2023	Integrated into India's national mmunization program in select states (2023)

Future Outlook for HPV Vaccination in India

1. **National Immunization Program:**
- With Cervavac's inclusion, India aims to vaccinate millions of adolescent girls annually, prioritizing high-risk states.

2. **Policy Advancements:**
- ◯Ongoing efforts to introduce HPV vaccines for boys and expand coverage to all adolescents will help reduce HPV transmission rates.

3. **Global Goals Alignment:**
- ◯By scaling up vaccination, India contributes to the WHO's goal of 90% HPV vaccination coverage by 2030 as part of the cervical cancer elimination strategy.

India's indigenous vaccine production and integration into public health programs are game changers. By addressing cultural, logistical, and financial barriers, India has the potential to become a global leader in cervical cancer prevention.

Conclusion :-

HPV vaccines have revolutionized cervical cancer prevention, yet their success depends on overcoming barriers to accessibility, affordability, and awareness. Through innovative outreach, partnerships, and sustained commitment, the dream of eliminating cervical cancer is within reach. By scaling up vaccination programs and integrating them into broader health initiatives, we can ensure a healthier future for generations to come.

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HPV
Vaccine


HPV
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FOR INJECTION ONLY
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02

THE ROLE OF DIAGNOSTICS: ADVANCED SCREENING TECHNIQUES FOR EARLY DETECTION

Author -Dr Vishnupriya KMN, MS, MRCOG, CIMP
Professor, Department of OBGYN,
St Johns Medical College, Bangalore

Dr Madhva Prasad, MS, DNB
Associate Professor, Department of OBGYN, St Johns Medical College, Bangalore

Introduction

The global public health burden of cervical cancer and the advances in its management and screening strategies are exciting success stories in the field of medicine, which is the theme of this booklet. This particular chapter focusses on the role of diagnostics with specific mention about the latest in HPV testing, advancements in Pap smear screening and the advent of point-of-care diagnostic tools. Innovation in the diagnostic techniques – resulting in reduced costs and better reach to the general population is the need of the hour. The emerging trends are summarized below. [1]

Screening techniques rely on one of the following steps

- Visual inspection of cervical abnormalities.
- Studying the abnormal exfoliative cytology
- Demonstration of HPV DNA

VISUAL INSPECTION: TO SEE IS TO BELIEVE

Visualization of cervix focusses on transformation zone and squamocolumnar junction. The most important advantage of direct visualization is the ability to take a diagnostic sample (cervical biopsy) at the point-of-care itself. This obviates the need for a second visit. Visualization is aided by acetic acid (cellular dehydration producing acetowhite areas in abnormality) or Lugol's iodine (detection of glycogen depletion producing unstained areas instead of mahogany brown in abnormality). Need for good quality lighting and good visual acuity of examining personnel are prerequisites. Cervical inflammation resulting in false positives and lack of permanent imaging or pathology for documentation of screening results are limitations of this method. [2,3] These techniques provide a good balance between accuracy and cost-effectiveness, especially in low resource settings. These techniques are explained further in Chapter 6.

When visualization is done with magnification and good optical resolution, it is termed colposcopy, which was described first in 1925 by Hans Hinselman (Germany). Scoring systems like Reid's and Swede's classification help better discrimination. [4]

Digital colposcopes offer much better resolution and accuracy and are being adapted by many institutions. However, for outreach activities, handy portable colposcopes are the main requirements. Portable colposcopes have the potential of revolutionizing these conventional techniques. Without compromising quality of visualization, these devices have the advantages of cloud storing of images and instant shareability of images. This helps healthcare professionals at the point-of-care to interpret images instantly and also consult experts (who may be at a remote location) enhancing the quality of counselling provided to the patient. Some newer devices

promise a turn around time of less than 10 minutes. [5,6] Feasibility studies have shown positive results and excellent accuracy has been reconfirmed by recent systematic reviews. [7]

Colposcopi

c visualization has been proposed to provide discrimination into high-risk vs low risk lesions, and aids in planning further management (histopathological diagnosis). Cost associated would be the main drawback of this method.

CYTOLOGY – PAST, PRESENT AND FUTURE

Cervical cancer screening has evolved significantly over the many decades from the conventional Pap smear described by George Papanicolau. While the first step still remains the Pap smear in most locations, many have moved towards the liquid-based cytology (eg BD SurePath) due to much superior accuracy parameters. [8] More importantly, the proportion of unsatisfactory smears is significantly lesser with the liquid-based cytology (3.7% vs 7.7%) [9]

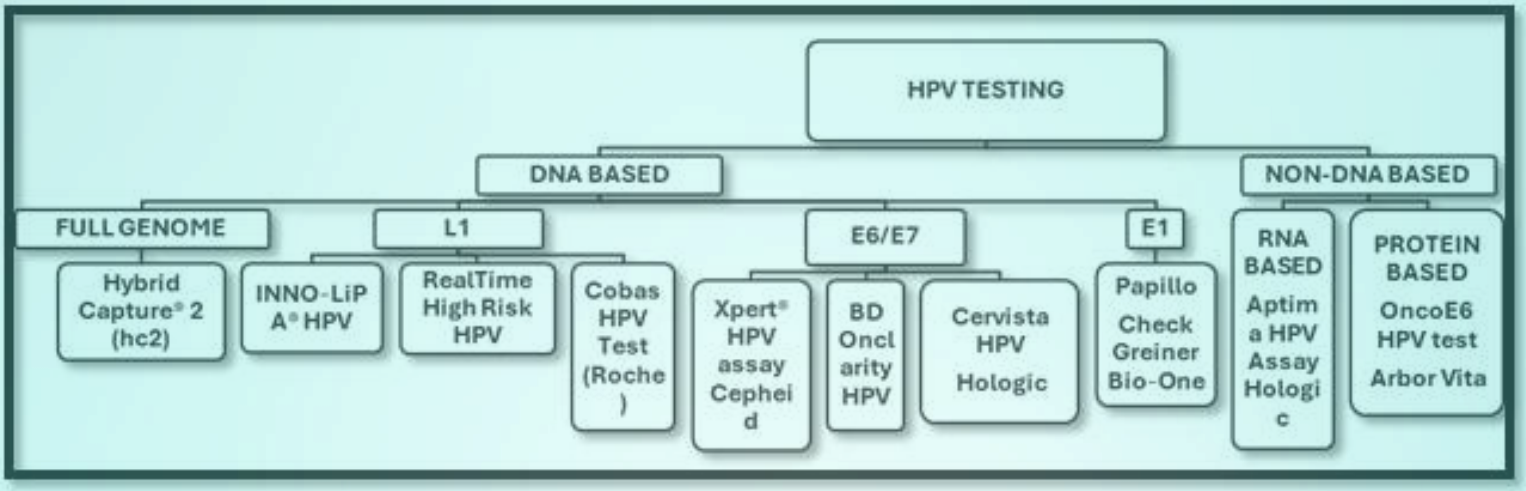
Digital analysis of cervical cytology images have improved the accuracy manifold. The initial introduction using the PAPNET system has now continued by systems like BD FocalPoint Slide Profiler, and ThinPrep Imaging Systems, with good accuracy performance and superior speed. [10]

· Reflex HPV refers to assessment of HPV in the same cytological sample that has been identified to have low-grade cytological abnormalities. It is particularly helpful when there is lesser clinical suspicion, and prompts better decision-making.
· Co-testing refers to apriori decision for testing of both HPV and cytology immaterial of each others' results. The decision for co-testing is usually made prior to sample collection itself. Clinicians must note the wide heterogeneity in various existing international guidelines. Clinicians should tailor-make their decisions based on local protocol and patient affordability. [11]

Artificial Intelligence and machine learning platforms are being roped in for enhancements in interpretation of cytology results and these are dealt with separately (Chapter 9).

HPV TESTING: THE LATEST INNOVATIONS

Demonstration of HPV products is the crux of this screening method. Commercially available HPV tests are based on the concept of identification/ demonstration of DNA, mRNA or proteins of the HPV. The DNA targets can in-turn be the entire genome, E6/E7 por L1 or E1. Alternatively, they can be classified based on full genotyping or partial genotyping. The accuracy and cost of the individual kits may vary based on the target and the number of genotypes tested. Figure 1 shows further details.
Figure 1. HPV testing methods and classification



These tests are made possible by the amplification of the small amount of genetic material obtained from the cytological sample. **Methods of amplification are summarized in table 1.**

Method of amplification	Elaborate name	Comments	Drawbacks
PCR	Polymerase Chain Reaction	Initial and well-established method.	Requires thermal cycler. Sensitive to PCR inhibitors Time consuming
IAT	Isothermal Amplification Techniques	Circumvents the drawbacks of PCR Operates at constant temperature Shorter time period Resistant PCR inhibitor	-
LAMP	Loop mediated Isothermal Amplification	Became popular during COVID pandemic. Coupled with colorimetric detection.	Sensitive to contamination, requires ideally sterile DNA-free and RNA-free workspace. Primers need special software.
RPA	Recombinase Polymerase amplification	PCR primers (complex combination of forward and reverse primers utilized)	Only one company has developed reagents – Cost prohibitive.

Considering the benefits of IATs being fast, inexpensive methods of amplification make them perfects tests for implementation in LMICs.

Point-of-care tests for human papillomavirus (HPV) detection: When the test results of HPV detection are available immediately, and can be communicated to the patient instantly, the test is classified as “point-of-care”. Though none of them have received approval from US-FDA, they are commercially available. These include care-HPV, onco-E6 Cervical Test, Xpert HPV, TruNAT HPV HR. Further studies on these are highly recommended.

Self-collection kits

Self-collection kits have been recently approved by US-FDA which allows individuals to collect their own vaginal/cervical sample, which avoids pelvic examination by a healthcare provider. It is believed to expand access, reduce barriers and improve screening rates, but may not potentially completely replace healthcare provider led care. [13] Such products (Cervicheck, M-Strip etc) have been approved by CDSCO, India also.[14]

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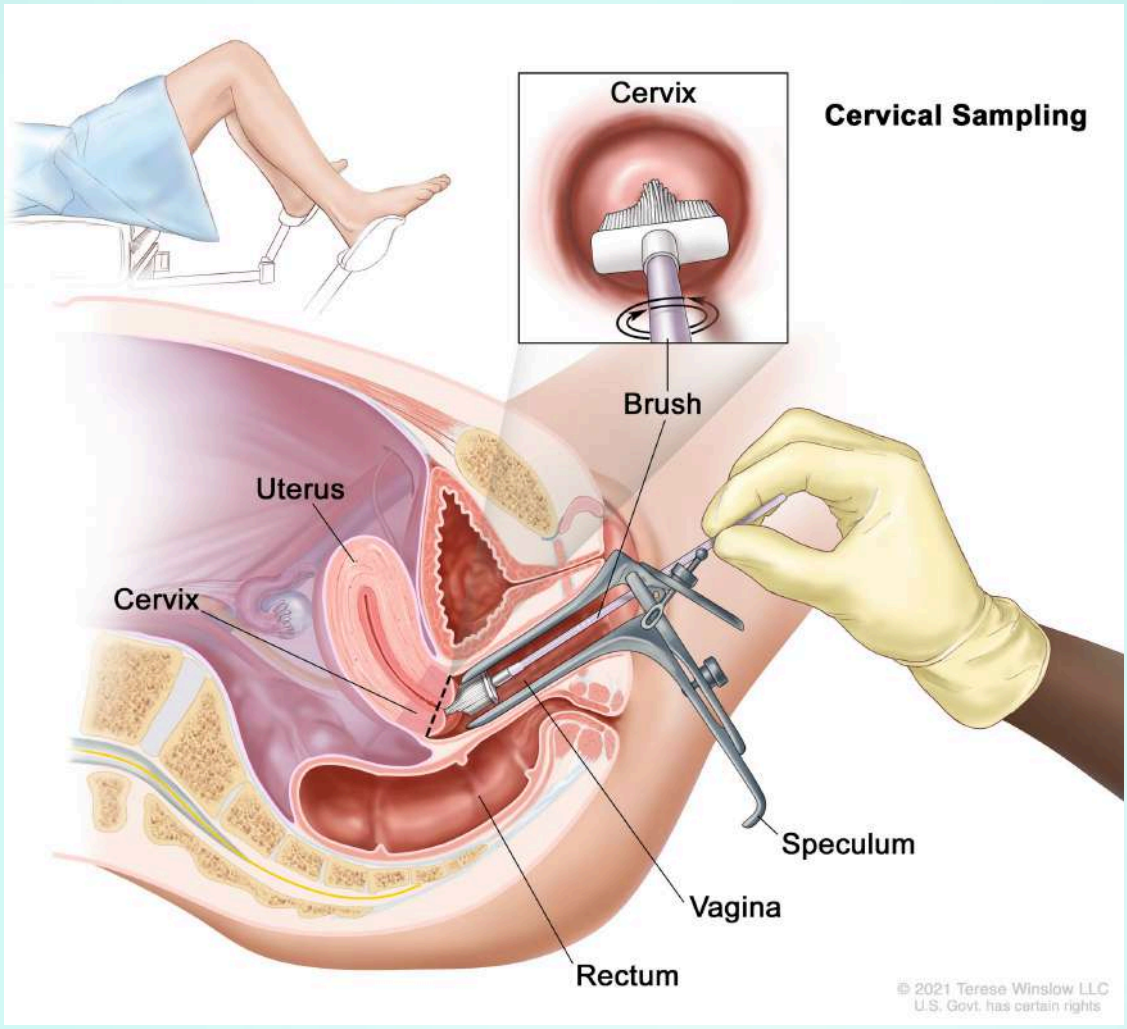
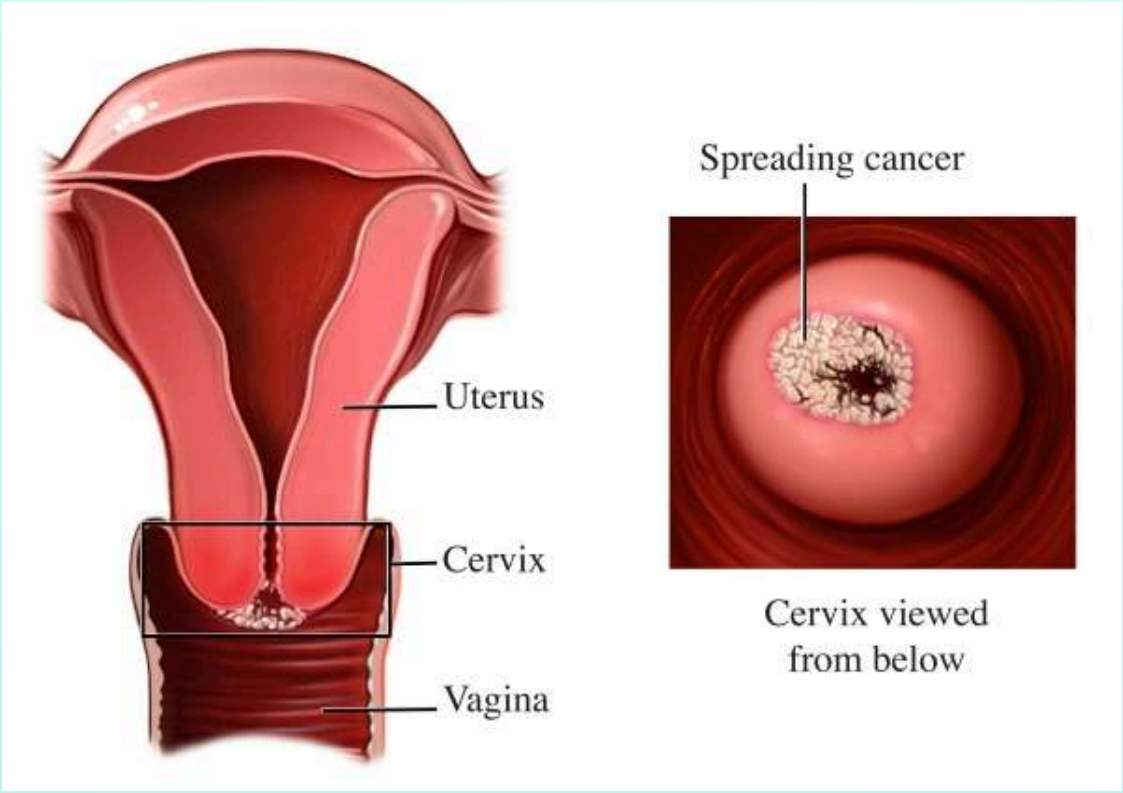


Cervical Cancer Screening



Cervical Cancer Screening and Test

03

Drugs That Fight Back: Advances in Treatment for Cervical Cancer

Author- Dr Sugandha Goel
President of Rotary Foundation Jodhpur 2024-2025
Secretary IMS Jodhpur Society 2024-25
Secretary Rotary Club Jodhpur 2025-26

Cervical cancer remains a major global health issue, particularly in low- and middle-income countries. Despite the advent of preventive measures like HPV vaccination and early screening, many cases are diagnosed at advanced stages, where therapeutic interventions become critical. Fortunately, recent developments in chemotherapeutic agents, immunotherapies, and targeted treatments offer new hope for better outcomes. This article discusses these advancements and their impact on cervical cancer treatment.

New Chemotherapeutic Agents

Traditional chemotherapy, particularly platinum-based agents like cisplatin, has been the backbone of cervical cancer treatment. However, the limitations of standard chemotherapy—such as toxicity and resistance—have driven the development of new chemotherapeutic strategies.(1,6)

Paclitaxel and Platinum-Based Combinations

Paclitaxel, in combination with cisplatin or carboplatin, has become a standard regimen for recurrent or metastatic cervical cancer. Studies, including those conducted by the Gynecologic Oncology Group (GOG), have shown improved survival rates with this combination compared to cisplatin alone. This approach has become the gold standard for first-line treatment in advanced stages.(2)

Gemcitabine as a Radiosensitizer

Gemcitabine is gaining traction as a radiosensitizer in cervical cancer treatment. By enhancing the effects of radiotherapy, it has shown promising results in improving overall survival. Trials like RTOG 0724 demonstrated the potential of adding gemcitabine to concurrent chemoradiation in locally advanced cervical cancer.(7)

Topotecan

Topotecan, a topoisomerase inhibitor, is approved for use in combination with cisplatin for recurrent or metastatic cervical cancer. Clinical trials have shown improved survival and symptom control compared to cisplatin alone.(2,8)

While these advancements are significant, they often fall short in resistant or recurrent disease cases. This gap has paved the way for immunotherapies and targeted treatments.

mmunotherapies: Revolutionizing Treatment

Immunotherapy has emerged as a transformative approach in oncology, including cervical cancer. It works by enhancing the immune system's ability to identify and destroy cancer cells, offering durable responses even in advanced stages.(4,5)

Immune Checkpoint Inhibitors

Checkpoint inhibitors target molecules like PD-1 and PD-L1 that cancer cells exploit to evade immune detection. These drugs have shown significant promise in cervical cancer:
Pembrolizumab: Approved for PD-L1 positive recurrent or metastatic cervical cancer, pembrolizumab demonstrated durable responses in the KEYNOTE-158 trial, with an overall response rate of 14.3%. Patients with high PD-L1 expression benefitted the most.(2,3)

Nivolumab and Atezolizumab:

These checkpoint inhibitors are under investigation and have shown potential when combined with other therapies like chemoradiation or bevacizumab.
Therapeutic Vaccines
Therapeutic vaccines aim to target the viral oncoproteins E6 and E7 of HPV, the causative agent of cervical cancer.(4,5)

VGX-3100: This DNA-based vaccine has shown promise in eradicating precancerous cervical lesions.

GX-188E: A therapeutic vaccine targeting HPV-16 and HPV-18 oncoproteins, it has demonstrated significant tumor regression in early-phase trials.

ISA101: When combined with checkpoint inhibitors, ISA101 enhances immune responses against HPV-associated malignancies.

Adoptive T-Cell Therapy

Adoptive T-cell therapy, including tumor-infiltrating lymphocyte (TIL) therapy, is an innovative approach where a patient's T cells are extracted, engineered, and reinfused to target cancer cells. Though still experimental, early results show potential for treating resistant cervical cancers. (8,9)

Targeted Treatments: Precision Medicine in Action

Targeted therapies aim to inhibit specific molecular pathways crucial for cervical cancer growth and metastasis, offering a more personalized treatment approach.

Anti-Angiogenic Agents

Angiogenesis is vital for tumor progression, and anti-angiogenic agents have shown significant efficacy in cervical cancer.

- Bevacizumab: The most established targeted therapy, bevacizumab inhibits VEGF, a protein that promotes blood vessel growth. The GOG-240 trial demonstrated that adding bevacizumab to chemotherapy improved overall survival in recurrent or metastatic cervical cancer.(1)
- Pazopanib and Cediranib: These oral tyrosine kinase inhibitors target VEGF receptors. Pazopanib, in particular, has shown disease stabilization in advanced cervical cancer.(1,2)

mTOR Pathway Inhibitors

The PI3K/AKT/mTOR pathway is often dysregulated in cervical cancer, making it a viable target.

- **Everolimus and Temsirolimus:** These mTOR inhibitors have demonstrated efficacy in preclinical models and are being evaluated in combination with chemotherapy in clinical trials.(1,2)

EGFR Inhibitors

Epidermal growth factor receptor (EGFR) is overexpressed in many cervical cancers. Targeting EGFR with monoclonal antibodies like cetuximab is being explored, particularly in combination with radiation therapy.(2,3)

Combination Therapies: A Multi-Pronged Approach

Given the complexity of cervical cancer, combination therapies are becoming the cornerstone of treatment strategies. They aim to maximize efficacy while minimizing resistance.(6,9)

- **Chemotherapy and Immunotherapy:** The KEYNOTE-826 trial showed that combining pembrolizumab with standard chemotherapy improved progression-free and overall survival in advanced cervical cancer.(2,3)
- **Immunotherapy and Anti-Angiogenic Therapy:** Combining checkpoint inhibitors with bevacizumab has shown synergistic effects, enhancing both immune response and anti-angiogenic activity.(1,4)
- **Radiation and Immunotherapy:** Radiation therapy enhances tumor immunogenicity, making it an excellent partner for immunotherapy in locally advanced cases.(5)

Emerging Therapies and Future Directions

The treatment landscape for cervical cancer continues to evolve with several novel therapies under investigation:

- Epigenetic Modulators: Drugs targeting epigenetic changes, such as DNA methylation and histone modification, are being studied for their potential to reverse resistance mechanisms.(8)
- Oncolytic Viruses: These engineered viruses selectively infect and destroy cancer cells, while stimulating immune responses.(9)
- Nanoparticle-Based Delivery Systems: Nanotechnology is being explored to improve the delivery and efficacy of chemotherapeutic and targeted agents.(9

Challenges and Opportunities

Despite these advances, challenges remain:

- **Access and Affordability:** High costs limit access to advanced therapies, particularly in resource-limited settings.
- **Biomarker Development:** Reliable biomarkers are needed to identify patients most likely to benefit from specific therapies.
- **Resistance Mechanisms:** Overcoming resistance to immunotherapies and targeted treatments is a critical area of ongoing research.

Future efforts must focus on equitable access, personalized medicine, and innovative combinations to further improve outcomes.

Conclusion :-

The advent of new chemotherapeutic agents, immunotherapies, and targeted treatments has transformed the management of cervical cancer, offering hope for improved survival and quality of life. As research continues to uncover the molecular intricacies of cervical cancer, the integration of these therapies into personalized treatment regimens promises a brighter future for patients worldwide.

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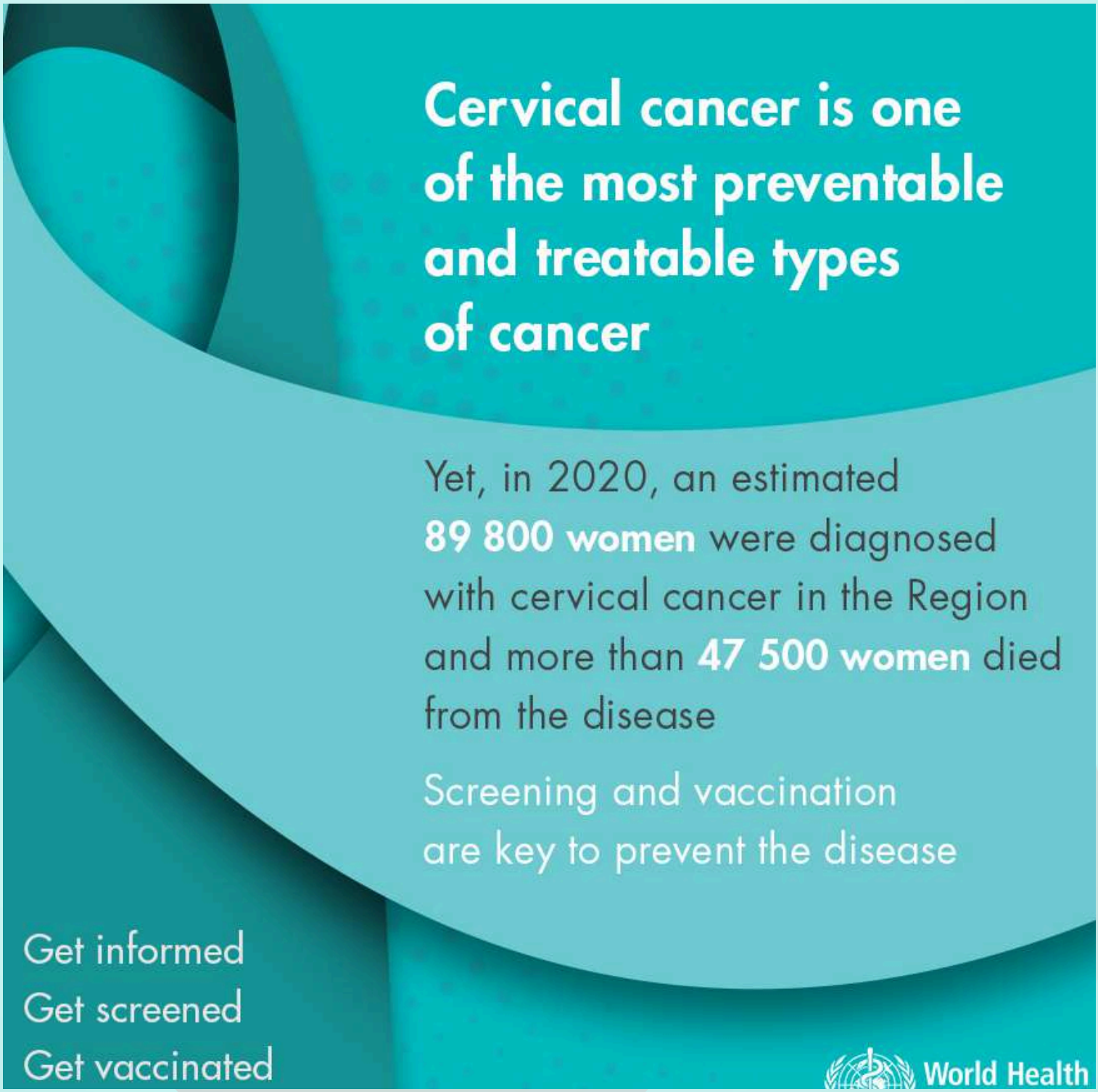
Cervical cancer is one of the most preventable and treatable types of cancer
Yet, in 2020, an estimated 89 800 women were diagnosed with cervical cancer in the Region and more than 47 500 women died from the disease
Screening and vaccination are key to prevent the disease
Get informed
Get screened
Get vaccinated
World Health

04 "Innovating Surgery: Medicosurgical Advances in Cervical Cancer Treatment" Focus on Data of Open, minimally invasive surgical techniques and robotics in managing cervical cancer.

Author- Dr. Rimpi Singla
ISCCP Chandigarh

Introduction:

The major limitations of International Federation of Gynaecology and Obstetrics (FIGO) 2009 clinical staging were inaccurate assessment of tumor size and inability to assess lymph nodes. The 2018 revised staging with division of stage IB into three sub-stages brought about a paradigm shift in management. Fertility-sparing surgery (FSS) is presently recommended for tumors <2 cm (FIGO 1B1) as the risk of recurrence is low (6%). Stage IB1 and IB2 tumors are likely to be cured by surgical treatment alone, while stage IB3 is best treated by chemoradiation. Further, adding a separate sub-stage IIIC for cases with LN metastasis segregates patients who appear to be operable based on clinical examination but would need subsequent adjuvant therapy because of positive LNs. This would prevent morbidity associated with multimodality therapy in most cases (1).

Updates in surgical approach:

Considering the universal advantages of Minimally invasive surgery (MIS) surgeons throughout the world adopted MIS radical hysterectomy with pelvic lymphadenectomy for stage I to IIA cervical carcinoma. Robotic surgery offers even better visualization, reduced operative time, and less blood loss than open surgery (2).

The results of the retrospective studies comparing oncological outcomes between MIS and open surgeries are conflicting. While some authors reported similar disease-free survival (DFS) and overall survival (OS) (3,4), others including a meta-analysis found that MIS hysterectomy was associated with shorter OS and DFS, and higher mortality (5-8). Then came the results of a landmark trial, the LACC trial (9), which made many international societies recommend caution while offering MIS. In this trial, 319 patients received MIS (84% laparoscopy, 16% robotic) and 312 underwent abdominal radical hysterectomy. MIS was associated with a lower 3-year disease-free survival (DFS) rate than open surgery (91.2% vs. 97.1%; HR, 3.74), and OS (93.8% vs. 99.0%; HR 6.00; 95% CI, 1.77–20.30). This prompted ESGO/ESTRO/ESP to recommend abdominal radical hysterectomy as the standard treatment for early cervical cancer, and that MIS may be considered only in low-risk tumors (<2 cm and free margins after conization), in high-volume centers experienced in performing radical hysterectomy with MIS after discussion with patient (10).

However, several limitations of LACC trial have been identified. The uneven distribution between laparoscopic and robotic-assisted cases (only 16%) (11) makes it challenging to draw definitive conclusions about robotic approach. Considering only 6 recurrences in stage

IB1 disease, which comprised 91.9 % of study population, the impact of the MIS approach on outcomes in low-volume cervical cancer remains uncertain. Further, subgroup analyses are needed to determine whether relapsing cases had specific histology, surgeon, and/or institution/country. The suboptimal outcomes with MIS may also be due to tumor contamination

because of uterine manipulators, colpotomy procedures, and pneumoperitoneum and carbon dioxide flow (12-14). Recent studies have indicated better outcomes by avoiding using uterine manipulators and vaginal sewing of the colpotomy (15,16).

Conization before radical hysterectomy:

Retrospective studies have indicated that conization before radical hysterectomy has been associated with a decrease in the risk of recurrences and yields favorable oncological outcomes (17,18). Preoperative conization was associated with a lower risk of tumor recurrence following laparoscopic radical hysterectomy as well (1.1 % vs. 16.1 %, $p < 0.001$) (19). The SUCCOR multicenter study (20) revealed 65 % reduction in the risk of relapse and a 75 % reduction in the risk of death in patients who underwent cervical conization before radical hysterectomy. In a recent study (21) among 238 patients treated with conization and subsequent simple hysterectomy, the survival was similar between open or MIS approaches. The positive impact of cervical conization may be attributed to a reduction in tumor volume. However, it is important to note that in clinical practice, cervical conization is more commonly performed on invisible or small tumors where the biopsy indicates a suspicion of invasion. As no randomized controlled trials are available to assess the influence on oncological outcomes, the routine practice of conization before radical hysterectomy is not recommended as a standard.

Updates in fertility-sparing treatment :

Fertility-sparing therapy can be offered to young patients with cervical cancer <2 cm (squamous cell carcinoma and HPV-related adenocarcinoma). Conization with negative margins is sufficient for stage 1A1 with no LVSI. For women with IA2-IB1 with no LVSI, depth of invasion <10mm, and no metastasis, conization with negative margins and pelvic lymphadenectomy or sentinel lymph node mapping is recommended. In the presence of LVSI, Radical trachelectomy + pelvic lymphadenectomy is required. Fertility-sparing therapy for patients with > 2 cm tumors carries a significantly higher risk of recurrence and should not be considered as a standard treatment.

Updates on extent of surgery for early-stage disease:

Radical hysterectomy with pelvic lymphadenectomy had been the preferred surgical approach. Several retrospective studies have indicated very low (<1%) probability of parametrial infiltration in low-risk (negative nodes, no LVSI, and a depth of stromal invasion of <10 mm) stage IB1 cervical cancer, which suggests that less radical surgery might be considered for this population.

In a landmark multicentre, randomized study, SHAPE Trial (23), involving 700 women with early-stage (lesions of ≤2 cm with invasion of <50% of stromal tissue or to a depth of <10 mm or both), simple hysterectomy (SH) including lymph-node assessment (2.52%) was non-inferior to radical hysterectomy (RH) (2.17%) for pelvic recurrence at 3 years. The incidence of urinary adverse effects was lower in the simple hysterectomy group. 50% of the hysterectomies were done laparoscopically (56% SH vs. 44% RH), and 25% robotically (24% vs. 25%). It is important to note that 281 (83%) of 338 patients in SH group had MIS approach

, leading many to deduce oncologic safety of MIS. On a post-hoc analysis of the SH group, the authors found no difference between MIS vs open approach for recurrence rate (4.3% vs 5.3%; p=0.73), recurrence-free survival or OS. However, the SHAPE trial was not designed to compare the surgical approach and the same was not even randomized. In addition, the low number of recurrence events and the low number of patients in both surgical groups did not allow adjustment for biases during a multivariate analysis. We need robust data from RCT specifically designed to make any recommendations on MIS.

Updates in sentinel lymph node (technique and recommendations):

Extensive pelvic lymphadenectomy may be safely avoided in a significant proportion of early-stage cases after sentinel lymph node (SLN) biopsy. A consensus statement on the surgical technique for SLN dissection in cervical cancer has recently been published. Experts agreed on the use of indocyanine green (ICG) as a tracer, superficial (with or without deep) injection at 3 and 9 o'clock, injection at the margins of uninvolved mucosa, grasping the cervix only in part which is free of tumor, identification of the ureter, obliterated umbilical artery, and external iliac vessels before SLN excision, grasping the node at the afferent/efferent channels (not at the center), commencing the dissection at the level of the uterine artery and continuing laterally, and completing dissection in one hemi-pelvis before proceeding to the contralateral side. A side-specific lymphadenectomy in the case of failed SLN mapping is recommended. The expert group also recommended against modifying

tracer concentration during re-injection after mapping failure, and removing nodes through port without protective maneuvers. Blue dye or radiotracer is acceptable when ICG is not available. According to ESGO/ESTRO/ESP guidelines lymph node assessment should be performed as the first step of surgical management and MIS is an acceptable approach for lymph node staging. The guidelines also promoted the use of a frozen section of SLN due to lack of benefit in completing radical surgery in node-positive patients. However, due to the debatable accuracy of frozen sections, some authors have proposed a two-step procedure with ultrastaging of SLN followed by radical surgery (24).

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Cervical cancer screening: Pap smears and the HPV vaccine

05 Making Screening Accessible: Mobile Clinics and Portable Equipment" Showcase portable colposcopy devices and initiatives making cervical cancer screening accessible in rural areas.

Author- Dr Sandhya Rani Panigrahy
MD, OG, FICMCH, FCGP, FICOG MICOG,FIAOG

Co Author - Anwesa Pal.
MBBS (HONS), MS (O&G), DNB (O&G),
Mch Resident gyne Onco AHPGIC

INTRODUCTION-Squamous cell carcinoma cervix is a cancer associated with high risk sub-types of the human papilloma virus (HPV) and represents a major public health burden worldwide. As per GLOBOCAN 2022[1] 6,60,000 new cases and 3,50,000 deaths occur due to carcinoma cervix worldwide. India contributes to 25% of all cancer cases. The cervical cancer elimination initiative suggests a three-pillar approach, as no single intervention will be enough.
The strategy requires accelerated action in prevention, screening and cancer management, to reach the following targets by 2030-90 % of girls fully vaccinated with HPV vaccine by 15 years of age70% of women are screened with a high-performance test by 35 and 45 years of age, pre-cancerous lesions are treated early
90% of women identified with cervical disease receive treatment (including treatment of cervical pre-cancer, and invasive cancer)
Now a days colposcopy is a powerful tool for properly identifying the transformation zone, grading lesions and taking biopsy from HSIL. The operator and the operational setting2 needs expertise for greater yield. “Smartscopy”3 is the digital mobile counterpart of conventional colposcopy. Recently, high-resolution images of mobile colposcopes are much preferred because they improve the detection rate and share images between supervising colposcopists and their trainees (usually junior cadre)4,5.Inspite of its high detection rate in cases of suspicious cytology there is limited availability in Lower middle income countries due to its high cost1.It is still cheaper than a fixed colposcope, and if available, it can be used in remote areas where traditional coloscopy was impossible. The Enhanced Visual Assessment (EVA) system (Mobile ODT Ltd., Tel Aviv, Israel) was developed to enhance visual inspection with acetic acid (VIA) procedures in resource-limited settings6,7,8.

METHODOLOGY-The MSU9 (Force Motors, Traveller & BSIII) provides Cervical cancer screening using VIA and immediate treatment using thermal ablation to provide the services. The MSU was designed with the front compartment for the sitting arrangement and with an elongated compartment at the back including 1.examination bed, 2.light source 3. wall-mounted clock 4.a platform to keep material for screening and treatment, sitting and storage area and a small wash basin.The vehicle has generator (900 VA) for providing treatment with thermal ablation. Screening to be done by colposcope and smartscope. A team is made of a medical officer, a community coordinator, a counsellor, a data entry operator, 2 nurses/nurse assistant/trained health care worker and a driver.Base level workers like CHO, ASHA worker and Staffs at LR were especially trained for screening and VIA. A WhatsApp group is created for the programme coordination and communication. Women with large lesions and those menstruating at the time of the screening are referred to higher centre for colposcopy, biopsy and treatment (ablation or excision). Awareness campaign is done using a laptop, speakers and an LCD.

Screening and treatment with thermal ablation are provided by trained nurses/ health care provider. With a cusco's speculum in a modified lithotomy position, 3-5% dilute acetic acid was applied on cervix with a sterile cotton swab and result was noted after one minute.Repeat test advised after

3years for VIA negative women. In VIA positive cases immediate ablative treatment with thermal ablation was done for the eligible lesions (when the lesion involves <3 quadrants of the cervix, no extension into endocervical canal or vagina, ectocervical growth with the squamo-columnar junction (SCJ) seen in its entirety without suspicion of invasion).Multiple overlapping applications are given for relatively larger lesion. Women treated with thermal ablation were followed up after 3months. All wastes are disposed of as per biomedical waste disposal guidelines and used specula were disinfected by autoclaving followed by 0.5% sodium hypochlorite solution for 20 minutes.

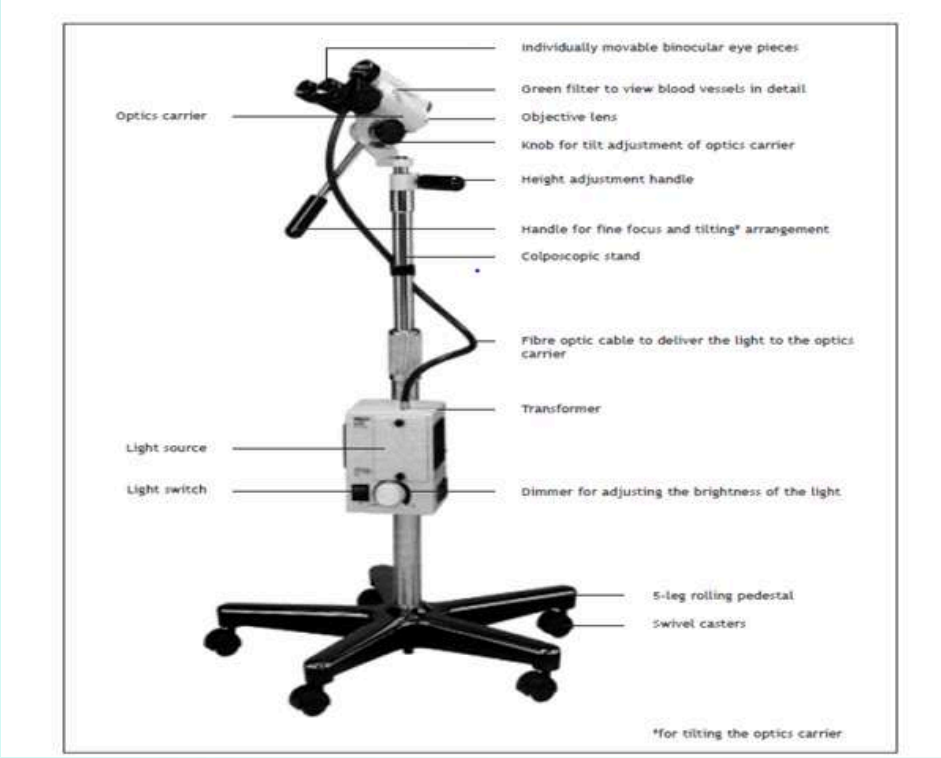
Role of ground level workers-Asha can be trained to do VIA or visual inspection in three condition
1. Abnormal bleeding 2. Post menopausal bleeding 3. Leucorrhoea
She will take the pics in a mobile, record and send to Medical officer .Abnormal pictures will be analysed further. Staffs working in LR too can be utilised for screening because they have an idea how normal cx looks like.Any abnormal looking cervix of reproductive age with symptoms or without symptoms to be screened and documented.It's an easy, time saving,cost effective, feasible and patient friendly alternative. It decreases the burden to already overworked centres.
DISCUSSION- We have demonstrated the feasibility of using an MSU .Use of MSU has been reported earlier specially for breast and cervical cancer screening across low, middle as well as high-income countries (Greenwald et al., 2017). Cancer screening in the family planning clinics are some of the other options (Mignot
et al., 2019) for improving screening coverage in India. It is also important that such programs are sustained and scaled-up to reach maximum possible number of women in the country. Ablative treatment in a 'screen and treat' program can be offered to women who fulfil certain eligibility criteria and visibility of the SCJ in its entirety is an essential element (WHO, 2013). Another important feature of the initiative is the use of thermal ablation for the treatment of screen positive women. Very few women who are screen positive and could not be treated in the MSU usually have > CIN 2 disease. Some patient may loss-to-follow-up due to limited time, unaffordable

transportation costs (The Lancet Oncology, 2020) and poor knowledge (Siddharthar et al., 2014), and public information campaign about the need for screening. Additional research is also needed in India to improve the adherence to colposcopy visits and appropriate treatment in the screen and treat programmes. We hope that cervical cancer prevention efforts are not stalled otherwise there will be substantial increase in the cervical cancer cases in the next 20 years. It is possible that countries that were planning to introduce an HPV test will have to re-think about its use and consider using VIA for cervical cancer screening which has considerable cost savings as compared to an HPV test.

NHS
The Newcastle upon Tyne Hospitals

transportation costs (The Lancet Oncology, 2020) and poor knowledge (Siddharthar et al., 2014), and public information campaign about the need for screening. Additional research is also needed in India to improve the adherence to colposcopy visits and appropriate treatment in the screen and treat programmes. We hope that cervical cancer prevention efforts are not stalled otherwise there will be substantial increase in the cervical cancer cases in the next 20 years. It is possible that countries that were planning to introduce an HPV test will have to re-think about its use and consider using VIA for cervical cancer screening which has considerable cost savings as compared to an HPV test.

Smart scope is a hand held portable colposcope with in-built LED and camera inside
(10x magnification) with a mobile screen.



Colposcope and its parts and pictures.

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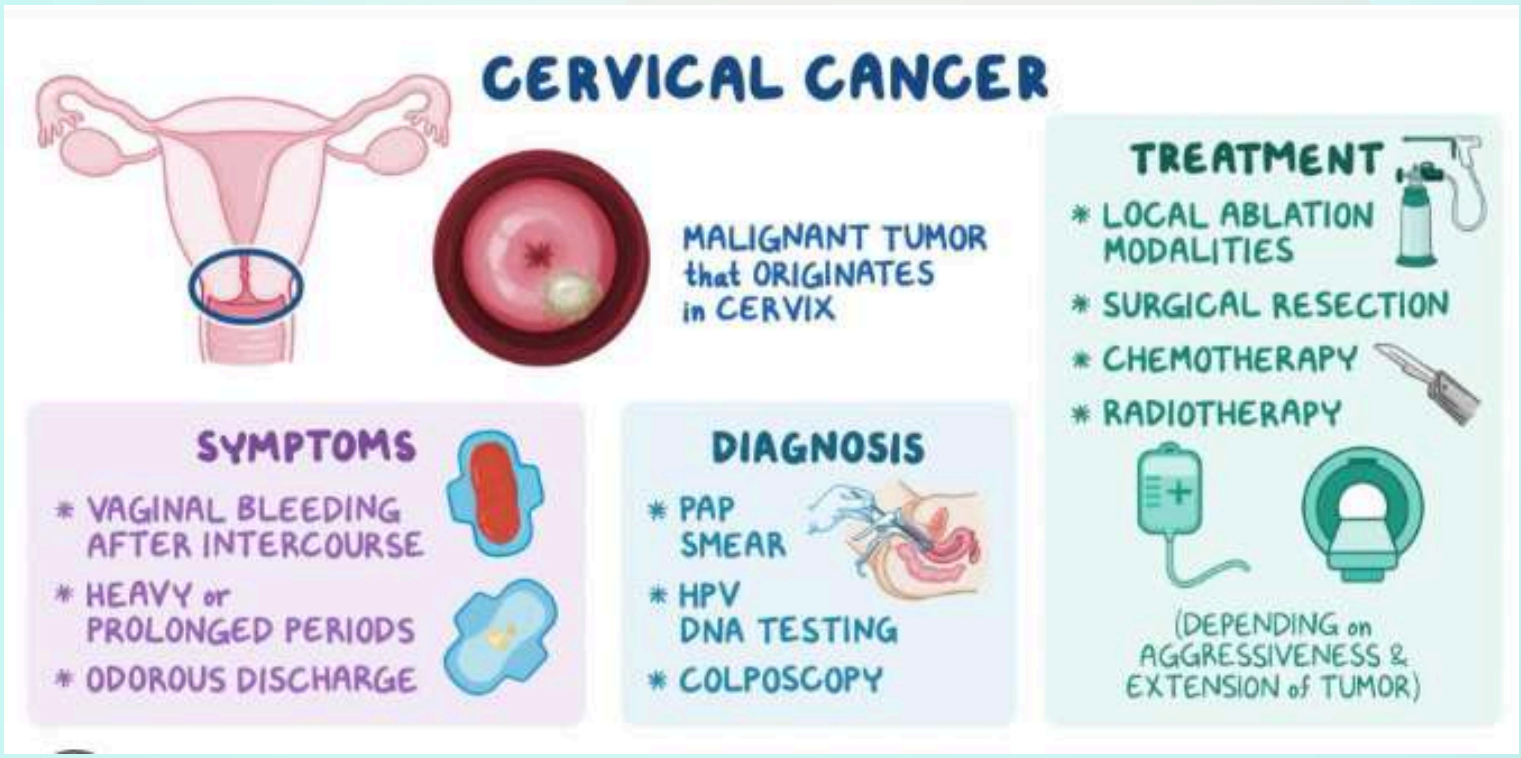
CERVICAL CANCER
MALIGNANT TUMOR that ORIGINATES in CERVIX
SYMPTOMS
* VAGINAL BLEEDING AFTER INTERCOURSE
* HEAVY or PROLONGED PERIODS
* ODOROUS DISCHARGE
DIAGNOSIS
* PAP SMEAR
* HPV DNA TESTING
* COLPOSCOPY
TREATMENT
* LOCAL ABLATION MODALITIES
* SURGICAL RESECTION
* CHEMOTHERAPY
* RADIOTHERAPY
(DEPENDING on AGGRESSIVENESS & EXTENSION of TUMOR)

06 "Bridging the Gap: Affordable Tools and Techniques for Low-Resource Settings".

Author- Dr Renu Jain
Professor, Department Of Obstetrics & Gynaecology, G.R. Medical College, Gwalior(M.P.)

Introduction

Widespread adoption of screening has led to dramatic decreases in the global burden of cervical cancer. However,
this decline has not been experienced equitably by all women worldwide. Those living in low- and middle-income countries and/or low-resource settings remain at increased risk for developing and dying as a result of cervical cancer, largely a result of a lack of access to routine screening and follow-up monitoring and treatment of dysplastic lesions.

Alternative approaches to diagnose cervical cancer at low-resource settings and in rural areas

Several strategies have been explored to diagnose cervical cancer in its early stage in the rural settings. Since the current concept of cervical cancer screening depends on the resources available, it may be adopted accordingly.

1.Cytology (Pap Smear)

It requires considerable infrastructure and funds along with repeated rounds of testing due to poor sensitivity. There is a need to enhance the efficacy and sensitivity of the cytological screening programme along with increasing the trained workforce in this field. Such a strategy needs to be adopted by our health managers for the National Cancer Control Programme.

2. Visual inspection

The high burden of cervical carcinoma and paucity of workforce in cytology in developing countries have led to screening by visual methods tests such as VIA and visual inspection with Lugol's iodine (VILI) and visual inspection with magnification devices-magnavisualizer (VIAM). Visual inspection-based methods that use existing (or minimal additional) human resources and require less training and fewer clinic visits.

An advantage of visual inspection-based approaches is that the immediate availability of screening results provides the opportunity to conduct a biopsy or offer treatment at the same visit (a screen-and-treat approach), reducing the likelihood of loss to follow-up.

3. HPV DNA testing

HPV testing has been accepted as the best screening test with highest sensitivity and negative predictive value. It is an adaptable method with the option of self-sampling and longer screening intervals. Despite the advantages, it requires standardized molecular laboratory settings and currently is expensive. Rapid HPV testing will reduce the reporting time and provide an option to screen and treat during the same visit.

Indigenous developments

Indigenous developments

·Indigenous innovations like portable colposcopes and HPV testing kits will further facilitate screening uptake. Newer innovations like battery-operated portable colposcopes and artificial intelligence-based software applications to detect and triage the pre-cancerous lesions are rapidly progressing and will be helpful to implement screening on a large scale

·The introduction of nucleic acid amplification testing at district/subdistrict hospitals and community health centers under the Free Diagnostics Service Initiative scheme can also facilitate HPV testing.

·Role of tumour markers-One inexpensive and easily affordable tumour marker which has been tried by different workers is AgNOR pleomorphic counts which showed rise with severity of cervical lesions. Application of AgNOR pleomorphic counts as a cheaper test to discriminate high-risk dysplasia cases whose immediate treatment will check the progression of the lesion to carcinoma. This will obviate the burden of follow up of all mild dysplasia cases which is a tedious problem and the selective follow up of high risk cases will definitely bring down the incidence of carcinoma cervix and associated mortality in the rural population.

·Role of biomarkers- Combined tests based on changes in epigenetic markers, miRNAs, and proteins might be the best choice to reduce the percentage of false positives without increasing the percentage of false-negative tests. Such integrated tests present technological challenges that must be met in order to allow their use in population-wide screening.

Management of premalignant cervical lesions in low resource setting

A critical component of any elimination strategy is to ensure access to safe, simple and effective treatment of premalignant lesions of cervix detected through screening. At least 10% of the CIN 2 lesions and 20% of the CIN 3 lesions will progress to invasive cancer, if left untreated . Due to such high risk of progression, immediate treatment is recommended for all high grade lesions unless detected in very young women or during pregnancy.

Cervical intraepithelial neoplasia (CIN) is a premalignant cervical disease that can be treated with either excisional (ie, conization) or ablative therapy. Given the resource requirements of excisional treatment methods, **the WHO recommends that ablative techniques be prioritised for eligible patients when available.**

The two primary ablative techniques recommended are cryotherapy and Thermal ablation.

Cryotherapy is an ablative technique that destroys tissue by freezing it using nitrous oxide or carbon dioxide gas. These gas-based units have been associated with inefficiencies in LMICs due to the continuous costs, procurement challenges and transportation issues of the gas tanks. The practical difficulties of cryotherapy (e.g. cost and supply of gas cylinders, equipment failure, and duration of treatment) has led to renewed interest in thermal ablation as an alternative ablative method for the treatment of screen positive women, especially in the context of screen and treat programmes.

·**Thermal Ablation**, also known as thermocoagulation and cold coagulation, is an ablative technique with comparable efficacy to cryotherapy that destroys tissue by heating it. The transformation zone of the cervix along with the lesion is destroyed using dry heat applied with a probe over 20 to 45 seconds. In 2019, Thermal ablation was endorsed by the WHO guidelines for the treatment of precancerous lesions in LMICs based on early evidence of safety and efficacy, and its simplicity of use in screen-and-treat strategies., also known as thermocoagulation and cold coagulation, is an ablative technique with comparable efficacy to cryotherapy that destroys tissue by heating it. The transformation zone of the cervix along with the lesion is destroyed using dry heat applied with a probe over 20 to 45 seconds. In 2019, Thermal ablation was endorsed by the WHO guidelines for the treatment of precancerous lesions in LMICs based on early evidence of safety and efficacy, and its simplicity of use in screen-and-treat strategies.

Eligibility criteria for thermal ablation :

1.fully visible SCJs and with SCJ positioned on the ectocervix (type 1 TZ). Location of the TZ inside the endocervical canal, partially or fully (TZ types 2 or 3), is an exclusion criterion of thermal ablation.

2.The lesion should not be occupying more than 75% (3 quadrants) of the ectocervix

3.The visible lesion on the cervix should not extend to the vagina or endocervix

4.There should not be any suspicion of invasive cancer

5.There should not be any suspicion of glandular abnormalities (on cytology, colposcopy or histopathology)

Thermal ablator device :-
The Liger thermal ablator incorporates a lithium-ion battery and an integrated electronic circuitry which controls the probe tip at the appropriate temperature for ablation (~100-120oC). The reusable probe (sizes 16mm, 19 mm flat, 19 mm nipple) has been designed to provide a non-stick surface and includes a stable hybrid circuit heating element, and
microprocessor control for safety as well as timing features. Each device kit is comprised of a handle, 4 probes (sizes 16mm, 19mm flat, 19 mm nipple), two lithium-ion rechargeable batteries, universal AC recharge adapter. Each probe is guaranteed to function optimally for at least 200 treatment cycles.

Procedure :-
WHO suggests that prophylactic antibiotics are not used when providing thermal Ablation Thermal ablation be provided at a minimum of 100 °C for 20–30 seconds using as many applications as needed to cover the entire transformation zone in overlapping fields.

Operation of Liger Thermal ablator unit

Activation (ON/OFF) Button: Press once to turn unit on. The activation button will illuminate green and one of the blue lights flashes to indicate unit is turned on. White illumination LED's on front of unit will also turn on. Press a second time to begin treatment cycle. The unit will shut itself off after the treatment cycle if needed.

Timer Lights: When the activation button is pressed a second time, the lights will all illuminate blue. After each ¼ of the treatment cycle is completed one light will turn off. An audio sound is also given to indicate cycle count down. When all timer lights are turned off the treatment cycle is complete and the unit shuts itself off. It has
commenced its cool down cycle. Oncethe cool down cycle is complete, the front white LED lights will turn off, and the probe may then be removed from the treatment area. If a second treatment area is needed, repeat the above steps before removing the probe.

Side effects- Pain, Vaginal discharge, Vaginal bleeding, Infection and vasovagal response are rare

Interval for followup :-
all women who have received treatment should receive post-treatment follow-up at 1 year to ensure effectiveness of treatment.

Advantages :-
·Outpatient procedure

·Can be performed by a variety of medical providers including primary health care workers
·Does not require anaesthesia.
·TA is relatively portable given its light weight
·Can be battery powered, enabling greater reliability in low-resource settings.
·As it does not use disposable parts or gas tanks, this method does not require continuous costs beyond maintenance, making it more feasible across healthcare settings, including community
care and rural contexts
·Electronic sensors within the applicator itself make it possible to have more reliable and stable final probe temperatures.
·Safe procedure with minimal complications with no effect on future fertility.

Disadvantages :-

·Ablation provides no pathologic specimen as the cervical tissue is destroyed. Therefore, these procedures are purely therapeutic and not of diagnostic value.
·They are appropriate only for select patients with previously well-characterized lesions histologically and colposcopically in whom invasive cancer has been excluded

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Symptoms of Cervical Cancer

Vaginal bleeding between periods or after menopause

Menstrual bleeding that is longer than usual

Bleeding after intercourse

Pain during sexual intercourse

Persistent pelvic and/or back pain

Pain during urination

Needing to urinate more often

Vaginal discharge that may be heavy and have a foul odor

Weight loss

07

"Empowering women through knowledge: educating for prevention and early diagnosis"

Author - Dr Himleena Gautam, MS, DNB, FMAS
Consultant, Apollo Hospitals, Guwahati
Contact number- 9678941859
Email- himleenaj@gmail.com

Introduction- January is the Cervical Cancer Awareness Month and we have a long way to go in spreading awareness among our women. Cervical cancer is the 4th cause of women's cancer worldwide, with 23% cases occurring in India[1]. 1 cancer death occurs every 7minutes with nearly 79900 deaths in 2022[2]. It is caused due to persistence of infection by high risk(oncogenic) type of human papilloma viruses(HPV), with types 16 & 18 causing 70% of the lesions. HPV infection is acquired during the reproductive years through mainly sexual routes and sometimes by non-sexual routes[3], with the age group of 16 to 25years being most vulnerable.

Importance of education and knowledge on cervical cancer- The irony of this whole situation is that cervical cancer is a totally preventable disease – by HPV vaccination and routine screening. However in both these components, India is lagging far behind. HPV vaccines(Cervarix & Gardasil) has been licensed in India since 2008 and Gardasil-9 since 2018. Yet, the use of these vaccines is minimal. Cervarix is no longer available and a cheaper, yet efficacious indigeneous alternative, Cervavac, has been introduced since 2022[4]. At the same time adequate screening using Pap smear/ Liquid based cytology, Visual inspection with acetic acid(VIA) and/or HPV testing are not being done routinely. Results from the fifth round of the National Family Health Survey(NFHS-5) 2019–2021 indicate that only 1.9% of women (aged 30–49 years) have ever undergone cervical cancer screening[5]. These are because of paucity of awareness, limited access to healthcare services, lack of trained healthcare providers, socio-cultural-religious beliefs, fear of adverse effects, financial constraints and gender discrimination[1,2,6,7,8]

Addressing the need for awareness- Overall awareness of cervical cancer is very low. Studies in various parts of world have shown that around 10-20% women are familiar with cervical cancer, HPV vaccine facts & pap smear[3,9,10]. Various studies in different developing countries have shown that community health educational interventions have increased awareness among women regarding cervical cancer, its cause, prevention and screening. Significant improvement in knowledge and agreeing to get vaccinated and being routinely screened are seen, through pre & post lecture questionnaires[11-16]. Considering that the ideal age of vaccination is 9-14years, extended upto 26years, it is very important that correct information and motivation are conveyed to the girl, as well as her parents and teachers[3,6]. The teachers can be recruited and trained to educate the girls and parents, and schools can be made a preferred venue for vaccine administration[6].Studies in US have shown that parental education about the HPV vaccine and their attitudes influence vaccine acceptability[7,17].

Role of medical professionals- various studies worldwide have shown that even medical fraternity has much less awareness for this cause[7,18-21]. FOGSI along with American Cancer Society(ACS) and Cancer Foundation of India(CFI) took the initiative of educating more than 10000 gynecologists across India through online platform in 2023-2024, which showed tremendous improvement in awareness among gynecologists regarding all the facts of HPV vaccination. IAP has simultaneously trained thousands of pediatricians for the same. These doctors have been given monthly task of taking up activities to create awareness and also provided posters to display in their clinics. "Mahila Kavach Kendra" has been created in many centres by FOGSI to make the vaccines easily available. Once the healthcare professionals are confident, they can be the best resource to educate the people in community, as they are trusted by the people and they convey accurate information, negating all the myths surrounding vaccinations. Research have shown that educating the medical and paramedical students can aid in HPV vaccine uptake[22,23]

Role of media- Newspapers, books, magazines, television, websites, various social media platforms etc can be of great use in educating all women regarding vaccine and co-testing. Local healthcare professionals can utilise the media to reach out to the people, making them understand in their own language. They can also use these platforms to educate regarding where they can get the vaccines, where they can go for screening and the costs associated. Utilising digital devices to deliver health education has been found to be beneficial[24,25].

Role of community health workers(CHW)- the rural population has more incidence of cervical cancer as compared to urban population. Thus, the educational interventions for use in rural population has to be distinctive and unique[25]. Evaluating the educational background of the women in a particular region and developing appropriate educational tools is important. Educational outreach program to firstly educate the CHWs and primary health workers, followed by helping them to deliver short, interactive learning sessions, to women in the community either one-to-one or in groups, sharing pamphlets, images and audio-visual materials in local language, can be very helpful[26-29]. Diverse audio-visual content and visual aid showing the reproductive anatomy, pictures of cervix and processes of screening, has been shown to increase comprehension, recall and attention to positively influence health outcomes[30,31]. Women should have the ability to ask questions, raise their concerns and express their preferences. Such tailored educational interventions have shown positive impact in informed decision-making by women[30]. According to WHO, community outreach and mobilisation are essential for cervical cancer screening education[32]. Studies have shown that interactive multimedia tools emphasizing empowering women were shown to increase patient satisfaction and preventive health behaviours[30,33,34].

To further enhance awareness, help of some NGOs can be taken like- Cancer Awareness, prevention and Early Detection(CAPED) trust, National Cervical Cancer Coalition(NCCC), GeBBS Foundation etc.

Role of Government & policy makers -

Lack of funding and conflicting healthcare goals pose hindrance to adequate screening and HPV vaccination. Thus comes the role of government. In 2016, the Government of India introduced a for the prevention and management of cancers. This initiative outlined guidelines for screening women aged 30–
65years using VIA after applying 3%–5% acetic acid, which is cost-effective for low-resource settings[35]. In the Interim Budget 2024, Union Finance Minister Nirmala Sitharaman have stated plans to concentrate vaccination of 9-14years old girls. Delhi launched a program in 2016 and pilot projects have been taken up in Punjab, Sikkim, Karnataka, Tamil Nadu, Chhattisgarh and Maharashtra, with Sikkim achieving 97% coverage
in 2018. The National Technical Advisory Group for Immunisation of India(NTAGI) has proposed introducing HPV vaccination in Universal Immunisation Program(UIP), but still not implemented yet[1,4]. In 2022, in a joint letter by the Union Education Secretary Shri Sanjay Kumar and Union Health Secretary Shri Rajesh Bhushan, the States/ UTs have been

equested to issue necessary directions at appropriate levels to ensure HPV vaccination. Once the governments make vaccines available free of cost or with minimal cost, the acceptability will further increase. When government makes it mandatory, the awareness also increases.

Conclusion- If HPV vaccination can be provided to 80-100% of target population along with 2 cervical screenings per lifetime by 2030, these can help in achieving cervical cancer elimination by 2070. Thus adequate awareness and education is the need of the hour, which can be achieved by collaborative efforts of healthcare professionals, community healthcare providers, NGOs, government organisations and the various media.

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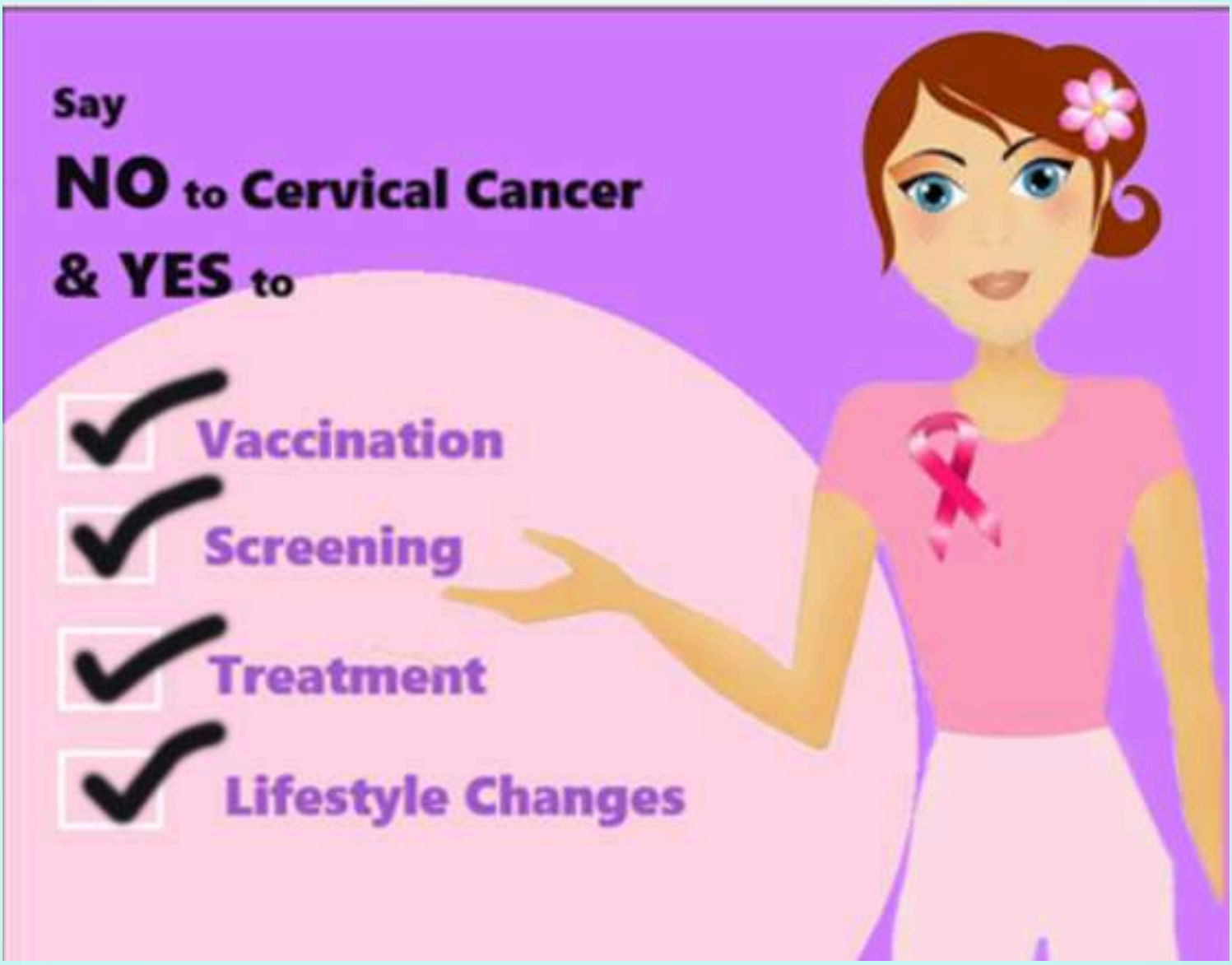

Say
NO to Cervical Cancer
& YES to
Vaccination
Screening
Treatment
Lifestyle Changes

08

The Digital Edge: AI in Diagnosis and Treatment Planning for Cervical Cancer

Author- Dr Okram Sarda Devi
Associate Professor, Department of OBG
Churachandpur Medical College, Manipur
Imphal Obstetrics and Gynecological society.

The term "artificial intelligence " was coined by John Mc Carthy in 1956.(1)

Cervical cancer remains a significant global health challenge, particularly in low- and middle-income countries (LMICs), due to limited access to early diagnosis and personalized treatment. With the advent of Artificial Intelligence (AI), a new era has emerged in the fight against cervical cancer, enhancing early detection, diagnosis, and treatment planning.

The World Health Organization's latest guidelines recommend three primary screening methods for the early detection of cervical cancer: HPV testing, cytology (encompassing both traditional Pap smears and liquid-based cytology), and visual inspection with acetic acid (VIA) (2).

The first commercial automated screening system, PAPNET, was introduced in 1992 (3) and was approved as a method for re-screening slides initially assessed as negative by cytologists. In 2004, the FDA approved the ThinPrep Imaging System as a commercial screening tool. This system utilizes a proprietary algorithm to identify the 22 most concerning fields of view (FOV). If abnormal cells are detected, cytotechnologists are required to manually examine the entire slide (4). In year 2010 - Neural Networks in Cytology Analysis was used and this integration of neural networks brought about significant advancements in analyzing cytology slides. These AI models began to surpass traditional diagnostic methods in speed and precision. In year -2015 - AI-Assisted Colposcopy where AI algorithms were employed to analyze images from colposcopy, enhancing the detection of cervical lesions and guiding clinicians in decision-making. By year 2020 - Personalized Radiotherapy with AI began where AI started assisting in personalized radiotherapy planning by analyzing patient-specific data, optimizing treatment protocols, and predicting outcomes.

Artificial Intelligence (AI) has significantly advanced cervical cancer screening, enhancing accuracy, accessibility, and efficiency. Here's an overview of its applications:

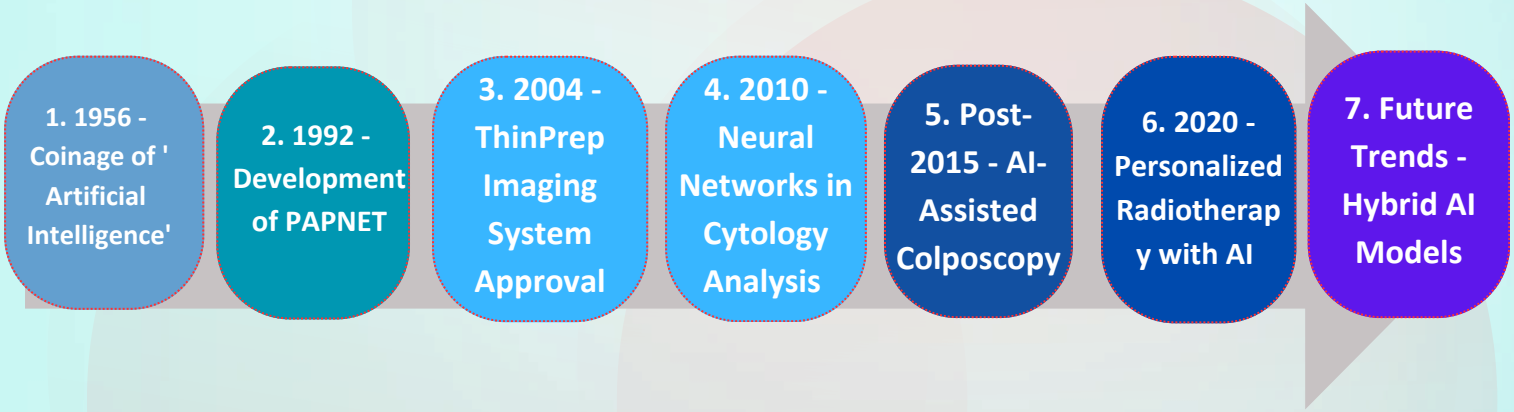
Role of AI in Cervical Cancer Management:

1. Screening and Early Detection:

A. Automated Cytology Analysis: AI-powered systems like neural networks analyze Pap smear images to detect abnormal cells with higher accuracy and speed. Reduces human errors and variability in cytological evaluations. Thereby, , processing of slides faster and helping in early and reliable detection of pre-cancerous changes.

Advantages of AI in cervical screening.

- **Improved Accuracy:** Reduces false negatives and false positives.
- **Scalability:** Extends quality screening to resource-limited settings.
- **Efficiency:** Speeds up the screening process, minimizing delays in diagnosis.
- **Cost-Effectiveness:** Lowers the cost of routine screening programs.



B. Visual Inspection with AI (VIA): AI algorithms, when combined with images from smartphone cameras or colposcopes, enhance the identification of pre-cancerous lesions, especially in resource-limited settings. Smartphone-based AI solutions for VIA screening in remote areas.

C. HPV Testing Integration: AI models can predict cervical cancer risk using data from HPV DNA tests and patient history. Prioritizes high-risk cases for further evaluation, enhances the predictive value of HPV tests. The use of AI to integrate result of papsmear along with HPV testing and clinical information's have reduced the referral to colposcopy

2. Diagnosis:
A. AI-Assisted Colposcopy:
a) AI algorithms analyze colposcopic images to identify cervical lesions.
b) Standardizes interpretation and reduces inter-observer variability
c) Higher detection rates for high-grade lesions.
d) Better guidance for biopsy decisions
e) AI technology significantly enhances the accuracy of lesion detection and biopsy during colposcopy, thereby reducing the likelihood of misdiagnosis (5,6).

B. Imaging Insights: AI tools analyze MRI, CT, or PET scans to pinpoint tumor location, size, and spread with greater precision, aiding in accurate staging. MRI has demonstrated exceptional accuracy in the preoperative staging of cervical cancer (7,8). The primary purpose of MRI is to assess peritumoral infiltration and detect lymph node metastasis (LNM) (8).

C. Histopathological Analysis: Machine learning models process digital slides to classify tumor subtypes and grade severity, reducing inter-observer variability

3. Treatment Planning:

A. **Radiotherapy Optimization:** AI algorithms predict the tumor response to radiation, customizing dose distribution while minimizing damage to surrounding tissues.

B. **Chemotherapy Personalization:** AI analyzes patient genomics and tumor characteristics to suggest optimal drug combinations and predict treatment outcomes.

C. **Surgical Planning:** AI-driven 3D modelling assists surgeons in visualizing tumor margins and planning minimally invasive procedures.

4. **Prognostic Prediction:**

A. **Survival and Recurrence Models:** AI leverages patient data to predict survival rates and the likelihood of
recurrence, enabling tailored follow-up care.

B. **Treatment and Side Effect Management:** Algorithms identify potential complications early hence, improving patient's quality of life.

Challenges and Considerations:

1. Data Privacy and Ethics: Ensuring secure handling of patient information.

2. Bias in Algorithms: Avoiding disparities in AI performance across diverse populations.

3. Integration with Clinical Workflows: Ensuring seamless adoption by healthcare providers.

4. Training Requirements: Equipping clinicians to use AI tools effectively

Conclusion:

AI enhances the specificity and accuracy of screening and diagnostic programs, addressing challenges such as time constraints and the shortage of skilled professionals. By minimizing bias from subjective factors, AI enables the implementation of cervical cancer screening in resource-limited areas, significantly reducing the disease's incidence. AI is revolutionizing the landscape

of cervical cancer care, from early screening to precision treatment planning. By harnessing the digital edge, healthcare systems can ensure better outcomes, reduced disparities, and a future where cervical cancer is detected early and treated effectively. However, a collaborative approach addressing ethical, technical, and practical challenges is essential to fully realize AI's potential in this domain.

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Cervical Cancer Treatment

The best protection is early detection. Get tested today. Encourage other women too.

09

The Future of Cervical Cancer Prevention: Emerging Vaccines and Beyond Next Generation HPV Vaccines and Their Potential to Eliminate Cervical Cancer Globally

Author- DR. ISHAN P. SHAH
MBBS; DGO; PhD; PGDCTM; PGDHM; BLSO
Joint Secretary – Mehsana Ob-Gy Society
Scientific Secretary – IMA Unjha

Cervical cancer, one of the most common cancers affecting women worldwide, is largely preventable through early detection and vaccination. In recent decades, the landscape of cervical cancer prevention has shifted dramatically with the development of vaccines targeting high-risk human papillomavirus (HPV) strains. However, as science progresses, the future of cervical cancer prevention is poised for even greater strides. Emerging vaccines and innovative technologies, along with a deeper understanding of HPV's role in cervical carcinogenesis, are offering promising avenues for reducing global cervical cancer burden.

Understanding the Role of HPV in Cervical Cancer

Human papillomavirus (HPV) is a group of more than 200 related viruses, and certain high-risk strains, particularly HPV-16 and HPV-18, are responsible for about 70% of cervical cancers. HPV is transmitted through sexual contact, and while most infections are transient and resolve on their own, persistent infection with high-risk HPV strains can lead to abnormal cell changes in the cervix. Over time, these changes can develop into cancer.

Screening programs like the Pap test (Pap smear) and HPV testing have significantly reduced the incidence of cervical cancer by identifying pre-cancerous lesions early. However, prevention remains the most effective strategy, and the advent of HPV vaccines has revolutionized the field.

The Current State of HPV Vaccines

The first generation of HPV vaccines, including Gardasil (Quadrivalent HPV vaccine) and Cervarix (Bivalent HPV vaccine), have already demonstrated remarkable success in preventing infection with HPV strains 16 and 18. Gardasil also protects against HPV types 6 and 11, which cause genital warts. These vaccines have been instrumental in reducing the incidence of cervical cancer, particularly in countries with comprehensive vaccination programs.

The vaccines are typically administered to young adolescents before they are sexually active, offering the most effective protection. As of 2024, many countries have implemented routine HPV vaccination as part of national immunization schedules for girls, with some expanding programs to include boys as well, given that HPV also causes other cancers, such as penile, anal, and oropharyngeal cancers.

Emerging HPV Vaccines and Next-Generation Developments

While the current vaccines are highly effective, ongoing research aims to improve HPV vaccination strategies. One promising advancement is the development of nonavalent vaccines, such as Gardasil 9, which protect against a broader range of HPV types, including five additional high-risk strains (31, 33, 45, 52, and 58). This expanded coverage could prevent an additional 20-30% of cervical cancers that are linked to these other HPV strains.

Researchers are also exploring new formulations of the vaccine to make it even more accessible and effective. For instance, intradermal vaccines, which use a smaller needle and less vaccine volume, could make immunization more cost-effective, particularly in low-resource settings.

Additionally, efforts are underway to create vaccines that offer longer-lasting immunity, reducing the need for booster doses.

Beyond traditional vaccines, the development of therapeutic vaccines—those designed to treat HPV infections or even early-stage cancer—is also gaining traction. These vaccines aim to stimulate the immune system to target and destroy HPV-infected cells before they can progress to cancer. Although still in early clinical trials, therapeutic

vaccines have the potential to offer a new tool in managing and even reversing precancerous lesions, providing hope for individuals with persistent HPV infections.

Beyond Vaccines: Innovative Prevention Strategies

While vaccines remain the cornerstone of cervical cancer prevention, other technologies and approaches are enhancing early detection and treatment, ensuring that even individuals who do not have access to vaccines can benefit from cutting-edge science.

1. Improved Screening Technologies: Advances in HPV testing have led to more accurate and less invasive screening methods. Molecular tests, such as the HPV DNA test, can detect high-risk strains of the virus with higher sensitivity than traditional Pap smears. These tests allow for more precise identification of women at risk for cervical cancer and reduce the need for unnecessary follow-up procedures.

2. Artificial Intelligence (AI) and Machine Learning: AI is being harnessed to analyze cervical cell samples with greater accuracy and speed than human pathologists. Machine learning algorithms can predict the likelihood of progression to cancer based on molecular and genetic data, which could lead to personalized treatment plans and more targeted interventions.

3. Global Vaccination Efforts: Access to HPV vaccines remains a significant barrier in many low- and middle-income countries. Global initiatives, such as the GAVI Alliance, are working to ensure that vaccines reach these underserved populations. Enhanced public health education campaigns are also crucial to raise awareness and dispel myths about the vaccine.

The Next Generation of HPV Vaccines

This broader protection could have a significant impact on global cervical cancer rates, particularly in regions where HPV types 16 and 18 are less common but other high-risk strains are prevalent. With the expanded coverage, the next-generation vaccine can address a larger proportion of HPV-related cancers, ensuring that more women, regardless of geographic location, benefit from vaccination.

1. Expanded Coverage: Nonavalent Vaccines

One of the most exciting developments in HPV vaccination is the introduction of nonavalent vaccines, such as Gardasil 9. Unlike earlier versions, which targeted only the two most prevalent high-risk HPV types (16 and 18), Gardasil 9 protects against an additional five high-risk HPV types (31, 33, 45, 52, and 58). These strains are responsible for an additional 20-30% of cervical cancers, meaning that Gardasil 9 has the potential to prevent approximately 90% of cervical cancer cases.

This broader protection could have a significant impact on global cervical cancer rates, particularly in regions where HPV types 16 and 18 are less common but other high-risk strains are prevalent. With the expanded coverage, the next-generation vaccine can address a larger proportion of HPV-related cancers, ensuring that more women, regardless of geographic location, benefit from vaccination.

2. Therapeutic Vaccines

While current HPV vaccines are preventative, there is a growing focus on the development of therapeutic vaccines—vaccines designed not to prevent infection but to treat existing HPV infections or precancerous lesions. Therapeutic vaccines aim to stimulate the immune system to recognize and attack HPV-infected cells before they can progress to cancer.

These vaccines work by targeting specific proteins produced by HPV in infected cells. The immune system, once activated by the vaccine, can destroy cells carrying the virus, preventing the development of cervical cancer. Therapeutic vaccines are still in early-stage clinical trials but hold enormous potential, especially for individuals with persistent HPV infections or early-stage precancerous lesions. If successful, therapeutic vaccines could provide a novel treatment approach, reducing the need for invasive procedures such as surgery or cryotherapy.

3. Longer-Lasting Immunity

Another key area of research is the development of vaccines that provide longer-lasting immunity, potentially eliminating the need for booster doses. Current HPV vaccines offer strong protection for several years, but booster shots are often recommended to ensure long-term immunity. New formulations under investigation aim to induce longer-lasting protection with fewer doses.

For example, some experimental HPV vaccines are designed to provoke a more robust and prolonged immune response by using novel adjuvants (substances that enhance the body's immune response to the vaccine) or by employing more efficient delivery systems. These improvements could make HPV vaccination programs simpler, more cost-effective, and more accessible, especially in low-resource settings.

4. Vaccination for Men and Boys

While cervical cancer primarily affects women, HPV also causes other cancers, such as penile, anal, and oropharyngeal cancers in men. Vaccinating boys as well as girls could have a dual impact: not only would it reduce the incidence of cervical cancer in women by preventing the transmission of HPV, but it would also reduce the overall burden of HPV-related cancers in both men and women.

Countries like Australia have already implemented routine HPV vaccination for boys alongside girls, and more countries are expected to follow suit. With increased global efforts to vaccinate both sexes, the potential to eradicate HPV-related cancers beyond just cervical cancer becomes a real possibility.

The Path to Global Elimination of Cervical Cancer

With the continued development of next-generation HPV vaccines, the global elimination of cervical cancer is becoming increasingly feasible. In 2020, the World Health Organization (WHO) launched an ambitious initiative to eliminate cervical cancer as a public health problem by 2030. The goal is to reduce cervical cancer incidence to
fewer than 4 cases per 100,000 women, which could be achieved through a combination of high HPV vaccination coverage, screening, and treatment of precancerous lesions.

The WHO's call to action is aligned with the potential of next-generation HPV vaccines, which could provide the additional protection needed to meet these targets. If vaccination programs continue to expand—especially in low- and middle-income countries where cervical cancer rates are highest—the global elimination of cervical cancer could become a reality within a few decades.

The United States, Australia, India, and Japan are launching a groundbreaking effort to help end cancer as we know it in the Indo-Pacific, starting with cervical cancer, a largely preventable disease that continues to be a major health crisis in the region, and laying the groundwork to address other forms of cancer as well. This initiative is part of a broader set of announcements made at the Quad Leaders Summit.

The Quad Cancer Moonshot will serve to strengthen the overall cancer care ecosystem in the Indo-Pacific by improving health infrastructure, expanding research collaborations, building data systems, and providing greater support for cancer prevention, detection, treatment, and care.
Quad countries intend to continue their strong commitments to Gavi including with HPV vaccines in the Indo-Pacific, with the United States making an early pledge of at least $1.58 billion over five years.
In addition, Quad countries will work together with United Nations agencies on bulk purchasing of HPV diagnostics to bring down the cost of cervical cancer screening, and work with the International Atomic Energy Agency to improve access to and quality of medical imaging and radiation therapy.
Project ECHO will accelerate cervical cancer elimination in the Indo-Pacific region through 10 new learning networks that facilitate effective and accessible prevention and care. More than 180 public health organizations in 33 countries leverage the ECHO Model, an evidence-based training and mentorship framework for community-based health care professionals, to improve cancer care delivery. By 2028, Project ECHO will launch at least 10 new communities of practice, with local partners and ministries of health in Indonesia, Vietnam, Malaysia, and

other Indo-Pacific countries to accelerate cervical cancer elimination, including programs for HPV vaccine implementation, treatment of precancerous lesions, and use of essential curative therapies.

Looking Ahead: A World without Cervical Cancer?

The future of cervical cancer prevention is promising, with emerging vaccines, improved screening, and cutting-edge technologies poised to reduce the global burden of this preventable disease. If current trends continue and vaccination coverage increases, cervical cancer could eventually be eliminated as a public health problem.
However, challenges remain, particularly in ensuring equitable access to prevention and treatment worldwide. It is imperative that efforts continue to expand vaccination programs, improve screening techniques, and support research into new vaccines and therapies. With continued innovation and global collaboration, the dream of a world free from cervical cancer may soon become a reality.

In conclusion, while we've made significant strides in cervical cancer prevention, the future holds even more promise. Emerging vaccines, novel treatment options, and improved access to healthcare are all critical pieces in the puzzle that could one day end the global threat of cervical cancer

Conclusion:-
The next generation of HPV vaccines, with their expanded coverage, potential for longer-lasting immunity, and development of therapeutic options, holds immense promise for the global fight against cervical cancer. By addressing both prevention and treatment, these vaccines could revolutionize the way we approach cervical cancer prevention worldwide. If the current momentum continues and vaccination efforts are scaled up, we may one day witness the eradication of cervical cancer as a public health threat—a victory that will have profound benefits for women's health around the world.

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